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REVIEW ARTICLE

Re-view and view on maturation disorders in the placenta

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Until delivery, the placenta plays an important mediator role between mother and fetus. This unit is affected by peristatic conditions, such as acute or chronic maternal diseases, malnutrition, drugs, and others. But also genetic factors and fetal malformations due to embryonic developmental disorders may contribute to macroscopically visible changes and functional disorders of the placenta. In a constantly ongoing progress of maturation, the placenta records and saves changes due to fetal distress partly as maturation disorders. Understanding of maturation disorders might, therefore, be an important contribution to a better understanding of influences on villous differentiation and might improve follow up and fetal outcome to reduce recurrence risk. However, an internationally unified classification system of maturation disorders does not exist. In this review, terminology, trials, and classifications of villous maturation disorders are summed up and compared, to pinpoint the need of agreement on an international unified and reproducible classification of maturation disorders.

Key words: Fetal outcome; histopathology; maturation and maturation disorders; pathology; placenta.

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NORMAL VILLOUS MATURATION ACCORDING TO GESTATIONAL AGE

Normal villous maturation is essential for optimized placental function adjusted to fetal demands of oxygen and nutrition. Ramification and maturation from predominating immature intermediate villi in the first and second trimester to the mature intermediate and terminal villi in the third trimester reflect dynamical adaptation processes.

Formation of tertiary villi finishes embryonic placental development. In the following weeks of pregnancy until delivery, villous maturation advances in linear villous growth and branching and transformation and differentiation of the stroma, fetal capillaries, and the villous trophoblast (chorionic epithelium). In detail, this process until term is characterized by (a) numeric villous growth and (b) villous ramification and differentiation of villi into four groups with different function: (1) Stem villi, with blood conducting, media containing vessels, surrounded by a contractile cell and fiber system. Main functions of stem villi are the regulation of blood flow and maintenance of tissue tonus to warrant mechanical stability of the villous tree. (2) Intermediate villi of central (immature) type are characterized by embryonic stroma with Hofbauer cells, few diffusely localized capillaries, and a nuclear rich two-layered villous trophoblast layer. These villi are assumed to represent the villous growth zone, with centripetal transformation into stem villi and centrifugal growth in length with increased branching (ramification). (3) Intermediate villi of peripheral (mature) type present a reticular and less collagen containing stroma with several centrally or peripherally localized capillaries, single-layered epithelium, and vasculosyncytial membranes. This villous type contributes to microcirculation, hormone production, and metabolic activity. (4) Terminal villi are characterized by blood supplying capillaries and venous sinusoides, each vessel tightly connected to the surface, several developed as vasculosyncytial membranes. Function of terminal villi is to exchange fetomaternal gas and

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nutritions and to take part in hormone production and metabolic activity (Figs 1A–C; 2A–D) (1).

Placental oxygen diffusion capacity increases from 1st to 3rd trimester until term up to 30-fold, due to reduced diffusion distance (2). The number of terminal villi increases from early pregnancy to term to about 60% (3).

VILLOUS MATURATION DISORDERS

Villous maturation disorders are described as focal or diffuse, qualitative and quantitative mismatch of villous ramification and tissue development, chronologically deviating from normal maturation for gestational age (1, 3–7).

Villous maturation disorders get manifest in mainly two sections of the villous tree: (a) Close to the immature intermediate villi which transform into stem villi, and (b) close to the transformation zone from the mature intermediate villi to terminal villi. Maturation disorders are more profound if they manifest in early development (3).

Maturation disorders are reported to be seen in small foci occupying less than 10% Medium Power Field (MPF) in 25% of placentas from normal sized and well-developed (eutrophic) fetuses without any known risk. In late pregnancy (gestational age 42 and later), maturation disorders are seen in 70% of placentas, occupying up to 50% of a MPF MPF. In placentas from preterm born children, maturation disorders are found in 90% of placentas, when associated with fetal growth restriction (FGR), histologically seen as diffuse change occupying more than 50% of a MPF (3).

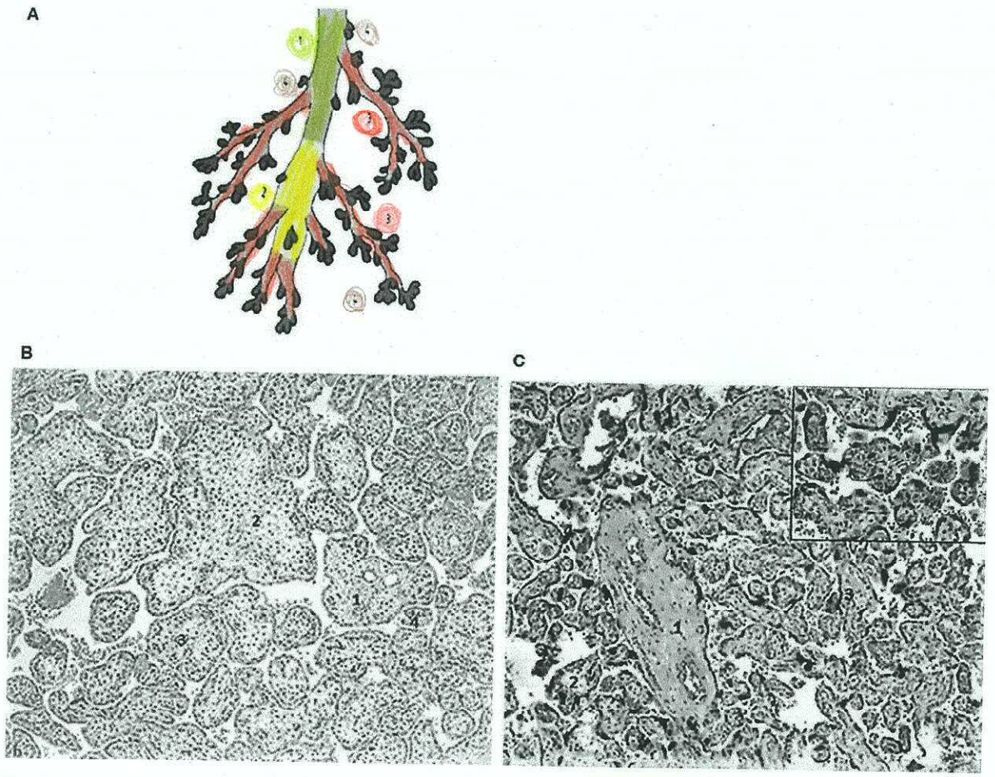

Fig. 1. (A) Illustration of the peripheral villous tree: Ramification into 1 stem villi, 2 intermediate villi of the central, immature type, 3 intermediate villi of the peripheral mature type, 4 terminal villi. (B) Histology of a placenta in gestational age 19. Villi of different size with loose stroma and few capillaries centrally localized. (C) Histology of a placenta in gestational age 38. Increased number of terminal villi with increased number of fetal capillaries (inlay shows higher magnification).

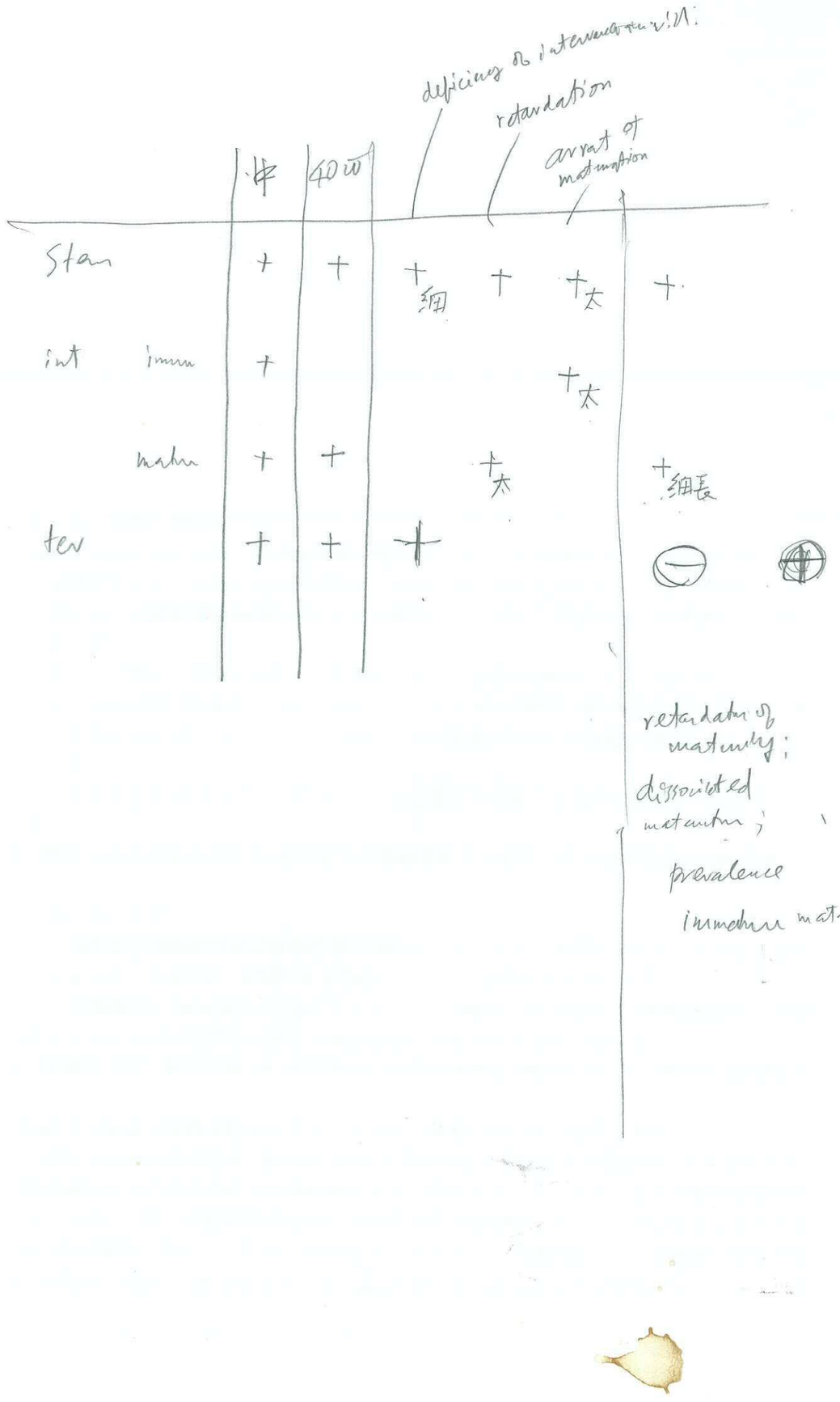

Table 1. German terminology of maturation disorders in comparison and Anglo-American terminology/descriptions

Becker (1981)	Kaufmann (1990)	Vogel (1984)	Schweikhart (1986)	Anglo-American
Maturitas iusta	Synchronous maturity	Mature according to gestational age	Synchronous maturity	Normal villous maturity
Maturitas tarda		Dissociated villous maturation disorder, prevalent mature	Asynchronous maturity	
Maturitas retardata	Deficiency of terminal villi	Retardation of villous maturation; dissociated villous maturation disorder, prevalent immature	Deficiency of terminal villi, peripheral villous immaturity	Delayed villous maturation (DVM), Distal villous immaturity (DVI)
Maturation arrest	Persisting immaturity	Villous maturation arrest	Persisting immaturity	Unspecific stroma edema
Maturitas praecox	Asynchronous maturity Hypermaturity	Preterm accelerated maturation	Hypervascularity	Accelerated maturation
		Deficiency of intermediate villi		Distal villous hypoplasia (DVH)
Chorangiosis Pseudochorangiosis Chorangiomatosis		Chorangiosis type I Chorangiosis type II		

reduction of the villous diameter and the level of maturation. Becker defined three groups with characteristic morphology of normal maturation and emphasized the chronological concordance between placental and fetal maturation (12–14). Based on this, he pinpointed typical mismatch of placental maturation, fetal maturation, and gestational age and classified maturation disorders chronopathologically as follows: arrest of villous maturation (maturitas arrest), dissociated maturation disorder (juvenile villi in mature placenta), asynchronic maturation including premature villous maturation and retarded villous maturation (maturitas praecox and maturitas retardata) (14). This was later revised and modified into maturitas iusta, maturitas tarda, maturitas retardata, maturitas arrest, maturitas praecox. Chorangiosis, pseudochorangiosis, and chorangiomatosis were added (15) (Table 1). Placental maturation and placental growth deviant from normal maturation for gestational age and fetal development were also reported by others (4, 16, 17). Villous maturation disorders were documented at any gestational age associated with clinically diagnosed maternal diabetes mellitus or preeclampsia (8, 18–22).

From these observations, Kloos and Vogel suggested a classification of maturation disorders, derived from morphology (23). They systemized maturation disorders as placental villi which deviate in quantity and quality and/or chronology from normal morphology according to gestational age. In consequence, they stated that the earlier the onset of the villous structural disorders, the more profound is the manifestation.

This detailed classification system was later simplified due to the results of histometric examinations (3, 24).

In 1984, Schweikhart suggested the term 'terminal villous deficiency', analogous to 'retardata and peripheral villous immaturity'. Furthermore, he suggested 'persisting immaturity', analogous to the term arrest, which was later subclassified into low, moderate, and severe grade. Asynchronous postterm maturity described a varying picture of immature and mature villi. He described hypermaturity as hypervascularity, which was later modified (25) (Table 1).

Chorangiosis is characterized by an increased vascularization of terminal villi. It is still unclear if this is a primary developmental disorder or a maturation disorder (26). Chorangiomatosis is interpreted as maldevelopment (27).

In the Anglo-American literature, Kaufmann and Benirschke suggested to differentiate maturation disorders of the villous vessels into branching and nonbranching angiogenesis in correlation to pre-, intra-, and postplacental hypoxia (28, 29).

Fox and Redline differentiated between 'preterm and delayed maturation disorders' and used the term 'irregular villous maturation', if both disorders were found in the same placenta (30–32).

Langston introduced the term 'distal villous immaturity' (DVI) (26), which was followed by the 'disorders of villous development' represented by DVI with placental overgrowth (DVIPO), and 'distal villous hypoplasia' (DVH) with placental undergrowth (DVHPU (33).

In recent years, villous developmental disorders associated with defined clinical maternal and fetal